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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/284,107	LOGTENBERG ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

MM

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/7/05 has been entered.

Status of Claims

Claims 1, 3, 5-10 and 13-18 have been cancelled.

Newly submitted claims 21-37 are pending and under examination.

Withdrawn Rejection

In view of the newly submitted claims and applicants arguments the following rejections are withdrawn:

35 USC 112, first paragraph with respect to the new matter and written description, as applied to the previous claims; 35 USC 112, second paragraph; the obviousness double patenting rejection; 35 USC 103 over de Kruif in view of Geysen and Granoff in view of the declaration (de Kruif of record). The

following rejections are maintained, as applied to the newly submitted claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly submitted claims 21-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A). New Matter Rejection:

The claimed method (f) of amplifying the polypeptide encoding-nucleotide sequences within the isolated packages (claim 21); oligopeptides that are non-linear (claim 31) or are continuous or discontinuous (claim 32) are all not supported in the original disclosure. The original disclosure does not disclose an amplifying method steps for the presently claimed genus, polypeptide. Neither does it provide clear support for

oligopeptides that are non-linear. This generic claim is not supported in the as-filed disclosure specific disulfide bridge.

Applicants point out support for the new claims, inter alia, page 6, line 33-page 9, line 25; page 10, lines 5-21; page 12, line 1-page 14, lines 15 and 19 -page 17, line 3.

A review of page 6, line 33-page 9, line 25 do not support for the amplifying step. It describes a linear or another conformation as ***for example*** a disulfide bridge circular peptides or unpredictable conformation. There is no clear support for a non-linear peptide. A disulfide bridge circular peptide is not a support for the broad scope of non-linear peptide which applicants state is an unpredictable conformation. The other cited sections relate to the same disclosure as the before-mentioned section. None of these sections disclose the term or definitions for a continuous or discontinuous peptide.

B). Written Description:

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

The claim recites for a method for obtaining the isolated nucleotide sequence of a polypeptide capable of binding to a specific oligopeptide from a target protein or a subregion

thereof comprising the recited steps. The disclosure at the time of filing does not describe the huge scope of the claimed components in the method. The disclosure does not describe the different aspects of the claims. There is no description of an isolated nucleotide sequence of a polypeptide. The disclosure does not describe the isolation of nucleotide of a polypeptide. Page 14, line 19 up to page 15, line 15, detail description, refers to a de Kruif publication that discloses a construct describing a synthetic scFv library. It does not disclose a nucleotide for this polypeptide. Even assuming, that this method produces a nucleotide, which it does not, the polypeptide isolated from encoding nucleotide is drawn specifically to a specific library construct of a fragment of an antibody (scFv). There is no correlation or relationship of the polynucleotide function to its structure and ability of encoding a polypeptide. Even for a defined nucleotide (which is not), it is known that the degeneracy of the gene code may not encode the polypeptide of interest. The detail description of a scFv is not an adequate description of the huge scope of the claims for antibodies or fragments thereof. A written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed genus

sufficient to distinguish it from other materials. University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993). The general description in the disclosure does not disclose or define a nucleotide sequence encoding any type of polypeptide. The general description provides a list of the antibody fragments e.g., Ig heavy and light chains, heavy-light chain, single chain antibody fragments and so forth. A "laundry list" disclosure of every possible moiety(species) does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species. In re Ruschig, 379 F.2d 990, 995, 154. The specification lacks a precise definition, as by structure, formula [or] chemical name of the huge scope of not only the claimed nucleotide encoding polypeptide but also of the other undefined components of the claimed method. For example, the target subregion to which the polypeptide is capable of specific binding; the kind, number or length of a set of overlapping or non-overlapping oligopeptides that can be derived form any type of target protein or a subregion; the library of polypeptides (not nucleotides). It is well established in our law that e.g., a library of polypeptides, albeit a complex one, requires that the inventor be able to define it so as to

distinguish from other materials. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQM 1961, 1966 (Fed. Cir. 1997); MPEP 2163. Applicant is further referred to the CAFC decision in the University of California vs. Eli Lilly and Co. CAFC 43 USPQ2d 1398 7/22/1997 with respect to adequate disclosure of the scope of the presently claimed components in the method. Adequate disclosure requires representative examples, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See In re Riat (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr. (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and University of California v. Eli Lilly and Co.. The more unpredictable the art the greater the showing required (e.g. by representative examples).

New claims 21-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in

the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include:

(1) the breadth of the claims,
(2) the nature of the invention,
(3) the state of the prior art,
(4) the level of one of ordinary skill;
(5) the level of predictability in the art,
(6) the amount of direction provided by the inventor,
(7) the existence of working examples, and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.
In re Wands, (U.S.P.Q. 2d 1400 (CAFC 1988).

1). The specification fails to give adequate direction and guidance in how to readily go about determining an isolated nucleotide encoding any antibodies or fragments thereof that is capable of specific binding to any target protein. It does not describe the kind, type, location and length of the overlapping and non-overlapping oligopeptides from the target protein. Nor does it describe derivation of said oligopeptide from a target protein or a subregion thereof that binds with an antibody of such specificity.

2). The specification failed to provide working examples for the numerous, broad components of the method.

3). The breadth of the claims encompasses a large diversity of nucleotide encoding polypeptide, even for antibodies, the determination of the sites of a target protein that forms a set to enable specific binding to an antibody. It is well known in the art, that it is often difficult to know which region of a given protein (target) can the antigenic determinant resides. Furthermore, the diversity of the library inserts is not easily estimated. It may be for example, that only a small subset of possible peptide sequences are presented efficiently by a particular expression system. And, it is not always easy to follow the expression of peptides in particular cells; for example, to know whether or not a specific cell is expressing a member of the insert, especially for biological methods.

4). The state of the prior art is such that a particular type of antibody can bind with specificity only to a specific antigen; that a library of polypeptides may not be expressed well depending upon the expression system use.

5). The art is inherently unpredictable because it is not possible to predict which antibody in the library can have said specific binding capability. It is generally known that the

conformational freedom i.e., discontinuous peptide that promotes binding might be restricted which may likely perturb the function and stability of the protein in ways difficult to predict and measure.

6). Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art that the numerous undefined components in a protein would result in specific binding of two compounds. Applicants' specification at page 17, lines 18-20 recognized that scFv preparations instead of phage preparation were used because the latter generated a high background in ELISA. Applicants do not adequately enable persons skilled in the art to readily determine the different undefined and broad components in the method. Applicants need not guarantee the success of the full scope of the claimed invention. However, skilled artisans are provided with little assurance of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Newly submitted claims 21-37 are rejected under 35 U.S.C. 103(a) as being unpatentable Burnie for reasons set forth in the last Office action.

Response to Arguments

Applicants submit that Burnie fails to teach or suggest each and every element of the claimed methods and therefore fails to anticipate the claimed methods. Applicants argue that the method disclosed by Burnie is complex and laborious requiring multiple steps of selection and more than one source of antibodies for the selection process. In contrast, the claimed methods are straightforward and simple, conferring the ability to isolate the nucleotide sequence to an antibody or antigen-binding fragment thereof specific for a discreet peptide on a large scale. The claimed methods lack any requirement for

immune antisera and are not limited by the identification of immunodominant epitopes. In other words, Applicants successfully omit numerous steps in Burnie's method to achieve a more efficient and ultimately more powerful method for the isolation of the nucleotide sequences of antibodies specific for a particular peptide sequence. See MPEP 2144.04(II)(B) note that the omission of an element and retention of its function is an indicia of unobviousness. According to Dr. de Kruif, the method of Burnie is distinct in many features, encompasses many additional steps, and multiple sources of antibodies are required. See Exhibit E. Therefore, Burnie fails to render the claimed methods prima facie obvious.

In response, the rejection is not under 102 rather, an obviousness rejection. There is nothing in the claims to preclude the steps recited in the Burnie reference. The claims recite an open-ended language "comprising" that does not preclude the presence of other steps present in the prior art method. It has been long held that the use of the term "comprising" leaves a claim open for inclusion of materials or steps other than those recited in the claims. Ex parte Davis, 80 USPQ 448. MPEP 2144.04 relates to an omission of an element in a composition. However, the element used by Burnie in the method is more specific than the instant broad components.

Applicants have not pointed out just exactly which element of the Burnie reference has been omitted to render the claim not prima facie obvious.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Brodin et al discloses identification of a target structures in vivo. See the specification at col. 3, line 25 up to col. 4, line 1.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0812. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
March 18, 2005